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E12-02 Recent Adv and Future Prospective in LC Pathology, Tue, Sept 4, 16:00 – 17:30

Cytology and fine needle aspiration biopsy in the diagnosis of lung cancer

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Conventional cytology such as sputum, bronchial brushes, washes and lavages and fine needle aspiration biospy (FNA) have long played a role in the diagnosis of primary and metastatic lung cancers. The separation of small cell lung cancer from non small cell lung cancer (NSCLC), especially in cytologic material, has historically been deemed sufficient for purposes of patient treatment. Small cell carcinoma was treated by chemotherapy and NSCLC underwent surgery first and then chemotherapy where appropriate. The separation of NSCLC into adenocarcinoma and its subtypes and squamous cell carcinomas was not necessary. In the era of targeted therapy this approach is no longer adequate.

Cytologic preparations can allow the distinction of adenocarcinoma subtypes, particularly bronchioloalveolar, and the recognition of squamous cell carcinoma.

The use of immunohistochemical stains such as TTF-1, CK7, CK20, 4A4, 34βE12 and p63 can be applied to cytologic material to help make these distinctions. In additon, cytology material such as cells blocks can be utilzed for EGFR gene mutation studies.

Specific cytologic findings associated with the presence of BAC or adenocarcinoma with a BAC component can be identified in cytologic preparatins. These findings include flat sheets of epithelial cells, nuclear inclusions and grooves and lack of prominent nucleoli.

The role of cytology in the diagnosis and management of lung cancer is of increasing importance and cytology can be used to provide excellent and accurate classifications of lung tumors.

E12-03 Recent Adv and Future Prospective in LC Pathology, Tue, Sept 4, 16:00 – 17:30

Intra-operative pathology consultation - novel approaches to frozen section

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Undertaking frozen sections (FSs) is a well-established and diagnostically accurate procedure that aids in the intra-operative staging of many cancers (1). The European Society of Thoracic Surgeons (ESTS) have recently published guidelines relating to intraoperative lymph node staging, and the pathologic evaluation of resected lymph nodes in patients with non-small cell lung cancer (NSCLC) with the aim of standardising management (2). A standardised approach to FS analysis of bronchial resection margins has also been recently proposed that highlights the difference between direct growth of invasive non-small cell carcinoma, lymphangitic spread and carcinoma-in situ (3)

In an effort to refine the above, there have also been recent studies assessing whether identification of sentinel nodes for frozen section may influence extent of resection and number of nodes required to be assessed during operation, with varying degrees of success (4,5).

The increased refinement of adenocarcinoma diagnosis in relation to the patterns identified in the WHO classification (6) and the Noguchi classification (7) has also led to groups assessing how far this can be taken at FS, as limited resection could be an acceptable alternative for some patients with Îearly Ì disease. One study has shown that, in small (< or = 10 mm) peripheral adenocarcinomas, FS may be used to apply Noguchi's classification, particularly types A and B, in which there may be intent to limited surgery (8). Using imprint cytology, there are also cytological factors that can predict invasion in small-sized peripheral lung adenocarcinoma with a bronchioloalveolar carcinoma component. In one study, univariate analysis identified five cytologic factors that were associated significantly with invasion (presence of tumour clusters comprising more than 50 tumour cells, nuclear overlap in more than three layers, presence of nuclear grooves, more than 3-fold variation in nuclear size, and 1 mitosis per 1000 tumour cells). Among these, nuclear overlapping in more than three layers and more than 3-fold variation in nuclear size were found to be independent predictive factors for invasion by multivariate analysis (9).

Another problem area, particularly in the lung, is when there is a history of previous malignancy. Differentiating primary from metastatic carcinomas can be difficult, especially with poorer morphology on FS and no histological feature is 100% specific (10). In paraffin-embedded tissue, an immunohistochemical panel is typically used to in addition to morphology to assess cytokeratin profiles (e.g. 7 and 20) and the presence/absence of more organ-specificÌ epitopes such as thyroid transcription factor-1 (TTF-1) and hormone receptors. Of these TTF-1 is the most valuable as it is highly specific and sensitive for primary lung tumours, excluding thyroid neoplasms (11,12). The ability to undertake intra-operative immunohistochemstry would therefore be of potential value as distinction of the type of tumour at this timepoint could influence surgery (anatomic resection for primary lung cancer and more localised resection for metastatic disease) (13,14) and methodology that permits this within the timeframe of a thoracotomy and with similar specificity and sensitivity to that seen for formalin-fixed tissues has recently become available (FSIHC) (15).

In a prospective study over two years, this additional immunohistochemical data at the time of operation increased diagnostic confidence in all cases, particularly in cases that were positive for TTF-1 (16).